

**REMARKS**

Claims 1-6, 8, and 14-29 were pending in the present application. Claims 8 and 14-29 have been cancelled herein without prejudice to their presentation in another application. Claim 1 has been amended herein, support for which can be found at, for example, page 5, lines 10-11 of the specification. New claim 30 has been added herein, support for which can be found at, for example, page 10, lines 15-20 of the specification. No new matter has been added. Upon entry of the present amendments, claims 1-6 and 30 will be pending.

**I. The Claimed Invention is Not Obvious**

Claims 1-6 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO 94/110165 (hereinafter, the “Harrison reference”) in view of Hagiwara et al., J. Med. Chem., 1994, 37, 2090-2099 (hereinafter, the “Hagiwara reference”) or Bernstein et. al., Bioorganic Med. Chem. Lett., 2001, 11, 2769-2773 (hereinafter, the “Bernstein reference”). Applicants traverse the rejection and respectfully request reconsideration thereof.

The Office alleges that it would have been obvious to modify the compounds of the Harrison reference according to the Hagiwara reference. The Office states “[W]hile not remarkably similar in structure, the compounds of Hagiwara teach that in the field of NK-1 receptor antagonists a substitution of naphthyl for phenyl is routine and desirable” (see, Final Rejection at page 29).

As a preliminary matter, the Office admits that the compounds reported in the Hagiwara reference are “not remarkably similar in structure.” This fact alone should be sufficient to indicate that one skilled in the art would not assume that one particular feature of a compound having structure A would necessarily be an appropriate substituted feature for a different compound having a different structure B, particularly when structure B is “not remarkably similar in structure” to structure A.

Further, the Office’s characterization of the Hagiwara reference is misguided. The Hagiwara reference **DOES NOT** teach, as the Office alleges, that substitution of naphthyl for phenyl is “routine and desirable” in the field of NK<sub>1</sub> receptor antagonists, as alleged in the Final Rejection at page 29. Although the Hagiwara reference reports that naphthylalanine was more

potent than phenylalanine, the Hagiwara reference also reports that (6-methylnaphthyl)-alanine and (6-chloronaphthyl)-alanine were **more than ten times less potent** than phenylalanine. *See* Hagiwara reference at page 2093. Applicants direct the Office's attention to amended claim 1, wherein the naphthyl ring is substituted. Further, the Hagiwara reference reports that the binding assay that resulted in naphthylalanine having increased potency over phenylalanine was **conducted at 4°C**, but when the assay was conducted at 25°C (i.e., room temperature), **naphthylalanine was less potent than phenylalanine**. *See Id.* Thus, the Hagiwara reference **DOES NOT** teach or suggest that substitution of naphthyl for phenyl is routine and desirable in the field of NK<sub>1</sub> receptor antagonists. The Final Rejection does not so much as even address these issues. Thus, the Hagiwara reference actually teaches away from replacing a phenyl with a substituted naphthyl, particularly when the resultant compound is desired to have activity at room temperature.

Teaching away is the opposite of the art's suggesting that the person of ordinary skill experiment in the claimed direction. A reference must be considered as a whole and the **portions arguing a teaching away from the claimed invention must be considered**. Thus, teaching away from the art is a *per se* demonstration of lack of *prima facie* obviousness. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988); *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); and *In re Nielson*, 2 U.S.P.Q.2d 1525 (Fed. Cir. 1987). The reports of the Bernstein reference (which is authored by some of the inventors of the present application and which was published less than one year before Applicants' priority date) does not overcome the teaching away of the Hagiwara reference. Accordingly, one skilled in the art would not be motivated to modify the compounds reported in the Harrison reference by the reports of the Hagiwara reference to obtain the compounds as claimed by Applicants.

In view of the foregoing discussion, Applicants respectfully assert that the claimed invention is not obvious and request that the claim rejection be withdrawn.

## II. The Claimed Invention is Enabled

Claims 8 and 14-29 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Although Applicants disagree with the reasoning set

forth in the Final Rejection, solely to advance prosecution of the present application, claims 8 and 14-29 have been cancelled herein without prejudice to their presentation in another application. Accordingly, the rejection is moot.

### **III. Obviousness-type Double-Patenting**

Claims 1-6, 8, and 14-29 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/539,140 in view of Elliot et al., *Bioorganic & Medicinal Chemistry Letters*, 2002, 12, 1755-1758 (hereinafter, the “Elliot reference”). The Final Rejection alleges that the instant claims differ from those of copending Application No. 10/539,140 by the identity of the moiety linking the naphthyl ring to the piperidine, and that this change is taught by the Elliot reference. The rejection is currently provisional; if the co-pending application is granted, Applicants may file the necessary disclaimer if and as appropriate.

In addition, claims 1-6, 8, and 14-29 are also provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/525,303 in view of the Elliot reference. The Final Rejection alleges that the instant claims differ from those of copending Application No. 10/525,303 by the identity of the moiety linking the naphthyl ring to the piperidine, and that this change is also taught by the Elliot reference. The rejection is currently provisional; if the co-pending application is granted, Applicants may file the necessary disclaimer if and as appropriate.

**IV. Conclusion**

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at 610.640.7859 to resolve any remaining issues.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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Date: **September 26, 2008**

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